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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,992	12/19/2001	David Bebbington	VPI/00-130-4	2621

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
05/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,992	BEBBINGTON ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,14,16,17,20,22 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,14,16,17,20,22 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20080219*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 19, 2008 has been entered.

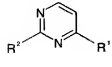
Claims 1-10, 14, 16-17, 20, 22 and 27 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

Claims 1-10, 14, 16-17, 20, 22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armistead et al., WO 01/60816. The reasons provided in the previous office action are incorporated hereby reference.

The reference, WO 01/60816 teaches a generic group of compounds of structural formula:  wherein R^1 and R^2 are, for example, NHR^3 wherein R^3 is optionally substituted aryl or heteroaryl. The reference further discloses a specific compound,

see the species of compound 35 in Table 1. The instant claims recite a genus of formula IIIc which differs from the reference disclosed compound by requiring a substituent at the 6-position of the pyrimidine ring which can be, for example, a methyl group. The reference compounds are taught to be useful as pharmaceutical agents having kinase inhibitory activity, which is the same use recited for the instant claims. One of ordinary skill in the art would have been motivated to pre pare the instantly claimed compounds that differ from the reference compounds by having a hydrogen in place of the methyl, with the reasonable expectation that such structurally analogous compounds would have similar properties and therefore, the same use as taught for the reference compounds, in the absence of a showing to the contrary.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that 'one of ordinary skill in the art would not have chosen compound 35 out of sixty exemplified compounds when Armistead provides more favorable compounds for inhibiting kinase'. This is not found to be persuasive. As explained above, the reference teaches a genus and discloses a species falling within the genus and the instantly claimed compounds differ by a single substituent from the reference disclosed compound. As submitted by applicant, the reference in fact teaches an activity for the disclosed compound 35, which in itself sufficient to one skilled in the art. One of ordinary skill in the art in possession of the reference disclosed compound 35, with the disclosed pharmacological activity would have immediately recognized that a single change in substitution such as replacing the hydrogen with a methyl group on the pyrimidinyl ring can be done without the loss of the pharmacological activity. A single change in substitution of the reference disclosed compound would have

resulted in a compound falling within the claimed structural formula IIIc wherein the pyrimidine ring is substituted at the 6-position with methyl group.

MPEP § 2144.09 provides that "A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979)". As provided above, it is clearly established that the instantly claimed compounds have very close structural similarity with the reference compound. Therefore, a *prima facie* case of obviousness is established.

Next, applicant argues that 'Armistead provides no motivation to modify compound 35 to arrive at the invention compound'. Applicant cites *Takeda v. Alphapharm* to support the argument. However, the situation is *Takeda* is different from the instant case. The court in that case ruled that 'one of ordinary skill in the art would not have been prompted to modify the reference compound, using the steps of homologation **and** ring-walking, to synthesize the claimed compounds'. Contrary to the cited *Takeda* ruling, in the instant application, one of ordinary skill in the art needs to modify the reference compound by substituting with methyl in place of the hydrogen to arrive at the instantly claimed compound represented by formula IIIc. One of ordinary skill in the art in possession of the reference compound, wherein the pyrimidine ring is unsubstituted at the 6-position, would have immediately recognized that the hydrogen could be replaced with a lower alkyl, e.g., a methyl (CH_3) substituent, without loss of the disclosed pharmaceutical activity. Applicant's argument that there is no specific teaching or

suggestion to modify the reference compounds is fully considered, however, "*KSR* forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness" *Ex parte Smith*, USPQ 2d (BPAI June 25, 2007).

It is maintained that one of ordinary skill in the art would have been motivated to modify the reference compound as indicated above, with the reasonable expectation that such structurally analogous compounds would have similar properties and therefore, the same use as taught for the reference compounds, in the absence of a showing to the contrary.

The following rejections are under new grounds:

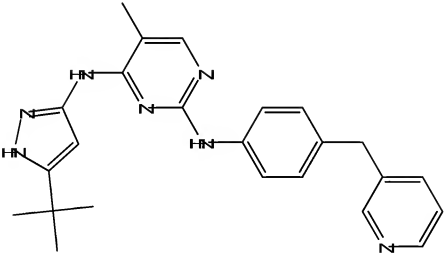
Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-10, 14, 16-17, 20, 22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dixon et al., WO 03/026664 (effective filing date September 26, 2001). The reference teaches a generic group of pyrimidine-2,4-diamine compounds, which embraces applicant's instantly claimed compounds. See formula (I) in page 7, and the corresponding species of the Examples. The compounds are taught to be useful as protein kinase inhibitors in the treatment of cell proliferative disorders, etc., see the abstract. The instant claims differ from the reference by reciting specific species or a more limited subgenus than the reference. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would

have similar properties and, thus, the same use as taught for the genus as a whole i.e., as therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Alternatively, the compounds according to the instant claims differ from the reference disclosed compounds by having a substituent at a different position on the pyrimidine ring from the reference compound. See the compound of Example 69 (depicted below for convenience):



The reference disclosed compound depicted above contains a methyl ($-CH_3$) substituent at the 5-position of the pyrimidine ring. The instant claims require that the 6-position substituent of the pyrimidine ring (R^3) to be a non-hydrogen substituent such as $-T-R^3$ wherein T can be a valence bond and R^3 can be a C_{1-6} aliphatic, e.g., methyl. Therefore, the instantly claimed compounds are positional isomers of the reference compounds as they differ from the reference compound

by the position of a substituent. It would have been obvious to one having ordinary skill in the art at the time of the invention to prepare the instantly claimed compounds because they are positional isomers of the reference compounds. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such isomeric compounds are suggestive of one another and would be expected to share similar properties and therefore, the same use as taught for the reference compounds, i.e., as pharmaceutical agents. It has been held that a compound, which is structurally isomeric with a compound of prior art is prima facie obvious absent unexpected results. *In re Finley*, 81 USPQ 383 (CCPA 1949); *In re Norris*, 84 USPQ 458 (CCPA 1950); *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990).

Note: Applicant's claim for domestic priority under 35 U.S.C. 119(e) based on U.S. Provisional Application 60/257,887 filed December 21, 2000 and 60/286,949 filed April 27, 2001 is acknowledged. However, the provisional applications upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for claims of instant application. Particularly, the provisional applications do not support the instantly claimed structural formula IIIc with the variables $R^{2'}$, L-Z-R^3, etc. Accordingly, the effective filing date for the instant application is December 19, 2001.

Receipt is acknowledged of the Information Disclosure Statements (3) filed on February 19, 2003 and copies are enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

May 22, 2008